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REMARKS

Claims 3, 7-13 and 16-18 are pending and under examination. Claim 3 has been amended to more distinctly point out that which the applicants regard as the invention. Applicants maintain that this amendment raises no issue of new matter. Accordingly, upon entry of this Amendment, claims 3, 7-13 and 16-18 will be pending and under examination.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 3 and 7-11 under 35 U.S.C. §103(a) as allegedly obvious over United States Patent No. 5,864,018 ("Morser") in view of Ritthaler et al. (Amer. J. Path., 146(3):668-694, 1995) ("Ritthaler").

Specifically, the Examiner asserts that it would have been obvious at the time of the invention to treat inflammation in a subject by inhibiting the interaction of AGE and RAGE by administering sRAGE or the anti-RAGE antibodies disclosed by Morser, because Morser demonstrates that sRAGE or anti-RAGE antibodies block the interaction between RAGE and its ligands and Ritthaler teaches that RAGE and its ligands are involved in the diseases involving inflammation.

In response to the Examiner's rejection of claims 3 and 7-11, applicants respectfully traverse. In order to find the claims obvious over Morser in view of Ritthaler, the prior art references, in combination, must teach or suggest all the elements thereof, and create both a motive to combine and a reasonable expectation of

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success. Morser and Ritthaler fail to do this.

Claims 3 and 7-11 provide a method for treating inflammation in a subject which comprises administering to the subject an agent selected from the group consisting of soluble receptor for advanced glycation endproduct (sRAGE) or anti-RAGE antibody or anti-EN-RAGE F(ab')₂ fragment in an amount which inhibits the interaction between receptor for advanced glycation endproduct (RAGE) and EN-RAGE, thereby treating inflammation in the subject.

Applicants maintain that Morser and Ritthaler combined fail to teach or suggest each and every element of the claimed invention.

Specifically, applicants maintain that nowhere does Morser teach a method of inhibiting inflammation in a subject which comprises administering an agent selected from the group consisting of sRAGE or anti-RAGE antibody or anti-EN-RAGE F(ab')₂ fragment in an amount which would inhibit the interaction between RAGE and *Extracellular Novel RAGE-Binding Protein (EN-RAGE)*. Applicants also maintain that nowhere does Morser teach or suggest the EN-RAGE polypeptide as a ligand of RAGE, or the role of RAGE/EN-RAGE interaction in inflammation-related pathology. Similarly, Ritthaler also fails to teach or suggest this element.

Additionally, applicants maintain that Morser, in view of Ritthaler, fail to create a reasonable expectation of success.

According to M.P.E.P. §2143.02, lack of predictability can serve as evidence that no reasonable expectation of success exists. Applicants note that numerous ligands (e.g. AGEs, amphoterin,

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amyloid fibrils, s100/calgranulins, etc.) are capable of binding to RAGE, resulting in a variety of consequences, of which inflammation is but one. Applicants maintain that, absent their experiments discussed in Example 3 in the specification, for example, Morser, in view of Ritthaler, do not create a reasonable expectation that the inhibition of the RAGE/EN-RAGE interaction would inhibit inflammation in a subject. Accordingly, applicants maintain that without knowledge of applicants' *in vivo* and *in vitro* experimental data in this application, one of ordinary skill would have no reasonable expectation that inhibiting the interaction of RAGE and EN-RAGE would succeed in treating inflammation in a subject. The Examiner's assertion of obviousness ignores this point.

Rather, the Examiner has applied an "obvious to try" rationale in support of the obviousness rejection. This rationale, which applicants do not concede even has a factual basis, is inadequate support for an obviousness rejection. (*O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988))

Accordingly, applicants maintain that the subject claims are not obvious over Morser in view Ritthaler, and therefore satisfy the requirements of 35 U.S.C. §103(a).

Further, the Examiner rejected claims 12, 13 and 16-18 under 35 U.S.C. §103(a) as allegedly obvious over Morser and Ritthaler in view of United States Patent No. 5,998,408 ("Baker").

Specifically, the Examiner asserts that it would have been obvious at the time of the invention to treat inflammation associated with autoimmune disease in a subject by inhibiting the interaction of

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AGE and RAGE by administering sRAGE or the anti-RAGE antibodies disclosed by Morser. This allegedly is because Morser demonstrates that sRAGE or anti-RAGE antibodies block the interaction between RAGE and its ligands, Ritthaler teaches that RAGE and its ligands are involved in the diseases involving inflammation and Baker teaches diseases involving inflammation, specifically the autoimmune process.

In response to the Examiner's rejection of claims 12, 13 and 16-18, applicants respectfully traverse the rejection of these claims.

Claims 12, 13 and 16-18 are dependant on claim 3 which is discussed above. Thus, these claims possess all limitations of claim 3.

The non-obviousness of claim 3, in relevant part, over Morser and Ritthaler is discussed above. Baker, which according to the Examiner merely teaches diseases involving inflammation, does not cure the deficiency of the other two references, in that it does not overcome the Examiner's failure to demonstrate that Morser and Ritthaler teach or suggest all the elements of the claimed invention and that the cited references create the existence of a reasonable expectation of success.

Accordingly, applicants maintain that the subject claims are not obvious over Morser and Ritthaler in view of Baker, and therefore satisfy the requirements of 35 U.S.C. §103(a).

Obviousness-Type Double Patenting Rejection

The Examiner provisionally rejected claims 3-11 and 16 as allegedly

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unpatentable under the judicially created doctrine of obviousness-type double patenting over claims 47, 50, 55-60, 62-65 and 67 of copending U.S. Application No. 09/167,705 in view of United States Patent No. 5,864,018 and Ritthaler et al. (1995). Applicants understand this rejection to apply to claims 3, 7-11 and 16. According to the Examiner, a timely filed terminal disclaimer in compliance with 37 C.F.R. §1.321(c) may be used to overcome a provisional rejection based on a nonstatutory double patenting ground.

In response, but without conceding the correctness of the Examiner's rejection, applicants will consider submitting a terminal disclaimer for claims 3, 7-11 and 16 once the rejection is no longer provisional.

Summary

For the reasons set forth hereinabove, applicants respectfully request that all the claims of this application be allowed, and that the application proceed to issuance.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

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No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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7/12/01

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